K122143

VENTANA®

A Member of the Roche Group

SECTION 6
510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92. The assigned 510(k) number is K122143.

807.92 (a)(1): Name: Ventana Digital Pathology
Address: 203 Ravendale Drive
Mountain View, CA 94043

SEP 19 2013

Phone: (408) 207-4201
FAX: (408) 207-4299
Contact: Mr. Mort Minaee

807.92 (a)(2): Device name- trade name and common name, and classification

Trade name: Virtuoso™ System for IHC PR (1E2)

Common Name: Digital pathology and image analysis system for immunochemistry-stained slides

Classifications: 21 CFR § 864.1860- Immunohistochemistry reagents and kits

Product Codes: NOT, NQN, OEO

807.92 (a)(3): Identification of the legally marketed predicate devices

This Virtuoso System for IHC PR (1E2) is substantially equivalent to its immediate predecessor with the same name, cleared under K111869 on March 5, 2012. The two Virtuoso systems are identical, with the sole difference being the automatic stainer that can be used with the reagents to stain the glass slides. The first PR submission qualified the Benchmark XT stainer, and this current submission qualified a second automatic stainer, the Benchmark ULTRA stainer.

807.92 (a)(4): Device Description

General Description

The Virtuoso™ System is an instrument-plus-software system designed to assist the qualified pathologist in the consistent assessment of protein expression in immunohistochemically stained histologic sections from formalin-fixed, paraffin-embedded normal and neoplastic tissues. The system consists of a slide scanner (iScan), computer, monitor, keyboard, mouse, image analysis algorithms for specific immunohistochemical markers, and software with a Windows web

Ventana Digital Pathology | 203 Ravendale Drive, Mountain View, CA 94043 |T: 408 207 4200|F: 408 207 4299
www.ventanadigitalpathology.com

browser-based user interface. Virtuoso is a web-based, end-to-end, digital pathology software solution that allows pathology laboratories to acquire, manage, view, analyze, share, and report digital images of pathology specimens. Using the Virtuoso software, the pathologist can view digital images, add annotations, make measurements, perform image analysis, and generate reports.

Hardware: The iScan slide scanning device captures digital images of formalin-fixed, paraffin-embedded tissues that are suitable for storage and viewing. The device includes a digital slide scanner, racks for loading glass slides, computer, scanner software, keyboard, mouse and monitor.

Software: The Virtuoso software is designed to complement the routine workflow of a qualified pathologist in the review of immunohistochemically stained histologic slides. It allows the user to select fields of view (FOVs) in the digital image for analysis and provides quantitative data on these FOVs to assist with interpretation. The software makes no independent interpretations of the data and requires competent human intervention for all steps in the analysis process.

Additional Materials Required:

- Ventana CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody
- Reagents for visualization, such as DAB chromogen
- Associated materials for completing immunohistochemical staining according to the appropriate package insert
- Color printer if user wishes to print color copies

Device Quality Control

The quality of results depends on the laboratory following the quality control instructions recommended in the labeling of the immunohistochemistry (IHC) reagents. The software also performs a quality check on the digital images to determine if they are suitable for further analysis using "Image Quality Assessment" algorithms.

Summary of Procedure

Samples are obtained as formalin-fixed, paraffin-embedded tissue blocks. Histologic sections are prepared and mounted onto glass slides. Slides are reacted with the PR (1E2) primary antibody, and are then visualized using DAB. Prepared slides are loaded into the Virtuoso system scanner and scanned. The resulting digital images are reviewed by the pathologist on a computer monitor, and appropriate fields of view (FOVs) are then selected for analysis by the Virtuoso software. The Virtuoso software produces a quantitative score for the FOV and an aggregate score over all the FOVs for the whole slide. The pathologist has the

Ventana Digital Pathology | 203 Ravendale Drive. Mountain View, CA 94043 |T: 408 207 4200|F: 408 207 4299
www.ventanadigitalpathology.com

choice of accepting the result or overriding with his/her own score for some or all FOVs.

807.92 (a)(5): Intended Use

The Virtuoso system provides automated digital slide creation, management, analysis, and viewing. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting, review and classification of tissues and cells of clinical interest based on particular morphology, color, intensity, size, pattern and shape.

The Virtuoso™ System for IHC PR (1E2) is for digital read and image analysis applications. This particular Virtuoso system is intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of progesterone receptor (PR) protein in formalin-fixed, paraffin-embedded normal and neoplastic tissue. This device is an accessory to Ventana Medical Systems, Inc. CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay. The CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay is indicated for use as an aid in the assessment of breast cancer patients for whom endocrine treatment is being considered (but is not the sole basis for treatment).

Note: The IHC PR (1E2) Digital Read and Image Analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and measurement of images from microscope glass slides of breast cancer specimens stained for the presence of PR protein. The pathologist should verify agreement with the Image Analysis software application score. The accuracy of the test results depends on the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody used to assure the validity of the Virtuoso System for IHC PR Digital Read and Image Analysis scores. The actual correlation of CONFIRM™ anti-PR antibody to clinical outcome has not been established.

Ventana Digital Pathology | 203 Ravendale Drive, Mountain View, CA 94043 |T: 408 207 4200|F: 408 207 4299
www.ventanadigitalpathology.com

807.92 (a)(6): Technological Similarities and Differences to the Predicate Devices

The following chart describes similarities and differences between the two test systems.

Characteristic	Virtuoso™ IHC HER2 (4B5) [Benchmark ULTRA Stainer]	Virtuoso™ IHC PR (1E2) [Benchmark XT Stainer] K111869
Intended Use/Indications for Use	This device is intended for in vitro diagnostic (IVD) use. The Virtuoso System provides automated digital slide creation, management, analysis, and viewing. It is intended for IVD use as an aid to the pathologist in the display, detection, counting, review and classification of tissues and cells of clinical interest based on particular morphology, color, size, intensity, pattern and shape. The Virtuoso™ System for IHC PR (1E2) is for digital read and image analysis applications. This particular Virtuoso system is intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of progesterone receptor (PR) protein in formalin-fixed, paraffin-embedded normal and neoplastic tissue. This device is an accessory to Ventana Medical Systems, Inc. CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay. The CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay is indicated for use as an aid in the assessment of breast cancer patients for whom endocrine treatment is being considered (but is not the sole basis for treatment).	SAME SAME SAME
Specimen Type	Formalin-fixed, paraffin-embedded tissue stained by immunohistochemical technique	Same
System Operation (Digital Read and Image Analysis)	Histologic observation by a pathologist through the viewer and image analysis systems	Same
Hardware and Software	Ventana iScan slide scanner, computer, color monitor, proprietary software for PR (1E2)	Same
Platform Components	mouse, keyboard, windows web browser.	Same
Primary Antibody (Assay) Reagent	Ventana CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody	Same
Ancillary Reagents/Stainers	DAB universal chromogen kits, Slides stained with Benchmark ULTRA stainer	DAB universal chromogen kits, Slides stained with Benchmark XT stainer
Localization of IHC positive stain	Nucleus	Same

Ventana Digital Pathology | 203 Ravendale Drive, Mountain View, CA 94043 |T: 408 207 4200|F: 408 207 4299
www.ventanadigitalpathology.com

807.92 (b)(1/2): Brief Description of Clinical Data (Non-clinical data N/A)

The Virtuoso System for IHC PR (1E2) with the Benchmark ULTRA stainer was clinically validated via a concordance study where approximately 120 cases were evaluated three ways by one pathologist at one site in a blinded fashion. Each case was scored (1) manually with a routine microscope, (2) as a digital image, and (3) by way of the image analysis application using a different order of slide presentation for each round. The manual score (reference result) was compared to both the digital read result and the image analysis result.

The data were evaluated as positive or negative for PR status using 0% to 0.99% positive staining as negative status, and at least 1% positive staininbg as positive status for both digital read and image analysis methods. The data for positive percent agreement, negative percent agreement, and overall agreement, plus the 95% confidence intervals, are shown below.

Digital Read

	Manual Microscopic Read		
Digital Read	**Positive**	**Negative**	**Total**
Positive	68	1	69
Negative	4	40	44
Total	72	41	113
Positive Percent Agreement (PPA) n/N (%) (95% CI)	68/72 (94.4) (86.6-97.8)		
Negative Percent Agreement (NPA) n/N (%) (95% CI)	40/41 (97.6) (87.4-99.6)		
Overall Percent Agreement (OPA) n/N (%) (95% CI)	108/113 **(95.6)** (90.1-98.1)		

Image Analysis

	Manual Microscopic Read		
Image Analysis Read	**Positive**	**Negative**	**Total**
Positive:	71	1	72
Negative:	3	39	42
Total	74	40	114
Positive Percent Agreement (PPA) n/N (%) (95% CI)	71/74 (95.9) (88.7-98.6)		
Negative Percent Agreement (NPA) n/N (%) (95% CI)	39/40 (97.5) (87.1-99.6)		
Overall Percent Agreement (OPA) n/N (%) (95% CI)	110/114 **(96.5)** (91.3-98.6)		

807.92 (b)(3): Conclusions from Clinical Testing

Concordance studies were performed for the Virtuoso System for IHC PR (1E2) with the Benchmark ULTRA stainer. The overall agreement between the digital read and the manual read was 95.6%, the overall agreement between image analysis and the manual read was 96.5%, and the predetermined acceptance criterion for each measurement of 75% has been met.

Ventana Digital Pathology | 203 Ravendale Drive, Mountain View, CA 94043 |T: 408 207 4200|F: 408 207 4299
www.ventanadigitalpathology.com

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

September 19, 2013

VENTANA MEDICAL SYSTEMS, INC.
C/O MS. ERIKA AMMIRATI
AMMIRATI REGULATORY CONSULTING
575 SHIRLYNN COURT
LOS ALTOS CA 94022

Re: K122143
Trade/Device Name: Virtuoso System For IHC Pr (1e2) Benchmark Ultra Stainer
Regulation Number: 21 CFR 864.1860
Regulation Name: Immunohistochemistry reagents and kits
Regulatory Class: II
Product Code: NQN, NOT, OEO
Dated: August 21, 2013
Received: August 22, 2013

Dear Ms. Ammirati:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Maria M. Chan -S

Maria M. Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved. OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on last page.

510(k) Number *(if known)*
K122143

Device Name
Virtuoso™ System for IHC PR (1E2)

Indications for Use *(Describe)*
The Virtuoso system provides automated digital slide creation, management, analysis, and viewing. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting, review and classification of tissues and cells of clinical interest based on particular morphology, color, intensity, size, pattern and shape.

The Virtuoso™ System for IHC PR (1E2) is for digital read and image analysis applications. This particular Virtuoso system is intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of progesterone receptor (PR) protein in formalin-fixed, paraffin-embedded normal and neoplastic tissue. This device is an accessory to Ventana Medical Systems, Inc. CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay. The CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay is indicated for use as an aid in the assessment of breast cancer patients for whom endocrine treatment is being considered (but is not the sole basis for treatment).

Note: The IHC PR (1E2) Digital Read and Image Analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and measurement of images from microscope glass slides of breast cancer specimens stained for the presence of PR protein. The pathologist should verify agreement with the Image Analysis software application score. The accuracy of the test results depends on the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody used to assure the validity of the Virtuoso System for IHC PR Digital Read and Image Analysis scores. The actual correlation of CONFIRM™ anti-PR antibody to clinical outcome has not been established.

Type of Use *(Select one or both, as applicable)* 801

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR ~~807~~ Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Yun-fu Hu -S